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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/001,220	11/15/2001	Alan John Kingsman	674523-2011	8450

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/001,220	KINGSMAN ET AL.	
	Examiner	Art Unit	
	Stacy B Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,9,10,13 and 16-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,9,10,13 and 16-21* is/are rejected.

7)☒ Claim(s) *5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed February 17, 2004 is acknowledged and entered. Claims 1-6, 9, 10, 13 and 16-21 are pending. The rejection of claim 13 under 35 U.S.C. 112, first paragraph is withdrawn in view of Applicant's amendment.

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Objections

3. Claim 5 is objected to for depending from claim 19.

Claim Rejections - 35 USC § 112

4. Claims 1-6, 9, 10, 13 and 16-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claims 1, 17 and all depending claims recite "producer cell". It is unclear what constitutes a producer cell. The specification discloses that retroviral producer cells contain all the elements necessary for the production of infectious recombinant retroviruses, see page 7,

lines 20-24. What are those elements? The producer cell must be defined by structural components rather than mere function.

b) Claim 1 and depending claims recite "enhancing the production", which is unclear. Previously, the Office withdrew a rejection under 35 U.S.C. 112, second paragraph over claims reciting "enhancing". Upon further consideration, this rejection is reinstated for the following reasons. While Applicant has provided a comparative basis for the relative term "enhancing", the specification does not clearly define what "enhancing" itself looks like. In other words, the claims should recite what kind of level of increased retroviral production is being achieved by enhancing its production (10-fold, for example). Without a clear definition of the level of enhanced production, one would not know whether the method is achieving "enhanced" production or an increase in production due to routine variation.

c) Claims 4, 18, 19, 20, 21 and all depending claims recite "gene product" and/or "transcription product". A gene product could be a cleaved nucleic acid residue, a gene, a single amino acid, an amino acid sequence, a peptide, a polypeptide or a protein. A transcription product could be a single amino acid, an amino acid sequence, a peptide, a polypeptide or a protein. It is unclear what is meant by these terms since "product" is not clearly defined.

d) Claims 1-6, 9, 10 and 19-21 lack complete method steps. While all of the technical details of a method need not be recited, the claims should include enough information to clearly and accurately describe the invention and how it is to be practiced. Generally, the minimum requirements for method steps minimally include a contacting step in which the reaction of the sample with the reagents necessary for the assay is recited, a detection step in which the reaction steps are quantified or visualized, and a correlation step describing how the

results of the assay allow for the determination. The instant method is drawn to a method for enhancing production of infectious retrovirus in a producer cell. The only step in the method is inhibiting the expression or activity of an endogenous receptor. The method should include steps that indicate that a producer cell was obtained with the necessary components for retroviral production, that the expression or activity of the endogenous receptor was inhibited and the method steps for inhibition, and that an infectious retrovirus was produced and isolated. The method steps should also include the separation of infectious retrovirus from non-infectious retrovirus, since both products would be expected to be present as a result of the method. Specific for claims 19, 5 (improperly depending from claim 19), 20 and 21, the method steps should include steps indicating that a vector with the desired gene was introduced into the producer cell. In summary, the method steps should show the required reagents to practice the invention, when to incorporate those reagents into the method, and an indication that "enhanced production" has been achieved by the determination of a defined level of production.

e) Claim 13 lacks complete method steps for the same reasons as claims 1-6, 9, 10 and 19-21 above. Additionally, the claim should include steps for making the infectious retrovirus replication-defective.

5. Claim 1 and depending claims are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to a method for enhancing the production of an

infectious retrovirus in a producer cell, comprising inhibiting the expression or activity of an endogenous receptor on the producer cell. The endogenous receptor is capable of binding the envelope protein of the retrovirus. The specification is limited to a description of endogenous receptors on human cells on page 10. Applicant has demonstrated how to down-regulate the amphotropic *pit2* receptor in 293T cells in Example 6. However, the claims encompass all endogenous receptors of all producer cells, which are not described in the specification. The specification fails to describe the full scope of the claims, namely, 1) endogenous receptors on non-human cells that bind viral envelopes, and 2) how to inhibit the expression or activity of endogenous receptors on human and non-human cells, other than 293T cells. Based on the specification, one would be limited to the down-regulation of the *pit2* receptor in 293 T cells. Applicant has only adequately described the down-regulation of the *pit2* receptor in human cells, but the scope of the claimed invention encompasses more than is described in the specification.

6. Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claim is drawn to a method for producing a pharmaceutical composition comprising infectious retrovirus that is replication-defective. The specification does not provide support for the administration of an infectious retrovirus alone, nor does the specification provide support for the retrovirus being the pharmaceutical composition. The retroviral vector carries a gene or genes that encode a pharmaceutical composition, but the retrovirus is only a vector, not the

pharmaceutical itself, see pages 14-16. The full scope of the claims is not supported by the specification.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 16 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Pedersen *et al.* (*J. Virology*, 1995, 69:2401-2405), herein referred to as "Pedersen". The claims are drawn to a producer cell whose endogenous receptor's expression or activity is inhibited, thereby blocking the binding of the receptor to a retroviral envelope polypeptide. Pedersen teaches chimeras of receptors for Gibbon Ape Leukemia virus (GALV)/Feline leukemia virus B (FeLV-B) and Amphotropic Murine Leukemia Virus (A-MLV). The chimeric receptors include Glvr1 (human receptor for GALV) and Glvr2 (human receptor for A-MLV), see abstract. Pedersen found that Region A from Glvr1 is sufficient to allow Glvr2 to function as a receptor for GALV in NIH 3T3 cells. Pedersen also found that chimeras encoding the Glvr2 form of Region A, and scrambling of the Glvr1 region A, abolished receptor function for GALV (page 2403, column 1, second full paragraph). Therefore, the claims are anticipated by Pedersen.

8. Claims 1-4 and 16-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Jabbar *et al.* (*Curr. Top. Microbiol. Immunol.*, 1995, 193:107-120), herein "Jabbar". The claims are

drawn to a method for enhancing infectious retroviral production in producer cells comprising inhibiting the expression or activity of an endogenous receptor on the producer cell, therefore blocking binding of the receptor to the envelope protein of the retrovirus. The endogenous receptor can be Pit1, Pit2 or CD4 and its co-receptors. The envelope polypeptide is amphotropic. The retrovirus can be a lentivirus. Also claimed is a producer cell whose endogenous receptor expression or activity has been inhibited.

Jabbar discloses that *vpu* down-regulates CD4 receptors on lentivirus HIV-infected cells and aids in virus release (pages 108 and 112). Since the definition of a producer cell is not clearly set forth (see rejection under 35 U.S.C. 112, second paragraph), and the definition of "enhancing production" is not clearly defined, Jabbar's cell qualifies as a producer cell since it has the elements necessary for HIV virion production, and the increased viral release of cells containing *vpu* compared to cells that do not express *vpu* is evidence of enhanced viral production. According to Jabbar, *vpu* naturally performs the function of virus release and CD4 down-regulation. The mechanism by which *vpu* aids in releasing virus and CD4 down-regulation is an inherent property of *vpu*. Therefore, the claims are anticipated by Jabbar.

Conclusion

9. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James C. Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SBC
Stacy B. Chen
May 13, 2004

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